REMARKS

A. Present Status of Patent Application

Claims 38, 54 and 104 are amended. Support for the amendments to claims 38, 54 and 104 is found at least at paragraphs 0011 and 0075 of Patent Application Publication No 2004/0156792.

New claims 107 and 108 are added. Support for these claims is found in the Patent Application Publication No 2004/0156792 at paragraph 0042 and Figure 1, and in the priority document (USSN 60/437,210).

Claims 23-37 and 84-102 had been previously withdrawn pursuant to a Restriction Requirement. Claims 38-39, 41, 44, 47-56, 58, 60, 62-68, 103-105 and 107-108 remain pending.

B. Response to Rejections

1. Provisional Double Patenting Rejection

Claims 1-8, 12-15, 19, 20, 38-44, 46-49, 52, 69-75, 77-79, and 82 were **provisionally** rejected on the ground of nonstatutory obviousness-type double patenting over the claims of co-pending U.S. application 11/187,757. To the extent the provisional rejection matures into a double-patenting rejection which is the sole ground of rejecting the present claims, consideration will be given to filing an appropriate terminal disclaimer.

2. Rejection under 35 U.S.C. §103(a)

Claims 38, 39, 41, 42, 44, 47-58, 60, 62-68 and 103-105 were rejected under 35 USC §103(a) over *Weers et al.* WO 01/85136 or US 2002/0037316. These rejections are traversed as to the pending claims.

Weers does not teach, suggest or disclose a particulate engineered for pulmonary administration wherein the particulate is formed of an active agent having a low solubility **specifically defined** as being between about 0.1 to about 1.0 mg/mL. Nor does Weers et al. teach a particulate engineered for pulmonary administration wherein the particulate comprises an insoluble particle having a geometric diameter of

less than about 3 microns and dispersed within a phospholipids matrix. Indeed, Weers et al **can not** teach or suggest such a claim limitation as of Weers et al does not relate to incorporation of discrete insoluble particles in a matrix.

Further, as applied to claims 104-105, Weers et al does not teach or suggest a particulate engineered for pulmonary delivery, comprising an active agent particle having a geometric diameter of less than about 3 μm and at least one property of a solubility in water of about 0.1 to about 1.0 mg/ml, or a low glass transition temperature (T_g) which comprises about 283°C, and a porous phospholipid matrix material.

Applicant contends that the Examiner's assertion that Weers et al teaches an active having a low T_g, is inaccurate, particularly with respect to the position that Amphotercin-B inherently has a low T_g. Weers et al does not teach or suggest actives having a low T_g; indeed, Weers does not address this parameter at all. Furthermore, if there is a relationship between a material's T_g and its solubility, such a relationship is complex, and not necessarily linear and predicable. Thus it cannot be predicated positively that a particular T_g is inherent in a material. Moreover, as applied to claim 104 (the only claim to incorporate a T_g limitation) the claim is **not** limited to amphotercin-B, thus the T_g recited therein **cannot** be said to be an inherent property of the claimed material. A low T_g is simply one parameter which qualifies materials as outside of the art when formulated in accordance with applicants' claims, to yield a dry powder suitable for pulmonary administration.

With respect to the Examiner's assertion that Weers et al's inclusion of lactose is does not serve to distinguish Weers et al. from applicants' claims, applicants have amended the claims to specifically exclude lactose. Notwithstanding such amendment, applicants continue to disagree with the Examiner's position that the phrase "consisting essentially of" does not exclude lactose. As recited by the Examiner, this well-known phrase excludes material which would affect the basic and novel characteristics of the composition. Applicants' specification clearly teaches that it is desirable to avoid certain excipients, especially bulking excipients such as lactose. (See Paragraph 0009-0012 of applicants' Specification). That being so, then the use of the phrase "consisting essentially of" clearly excludes that which is undesirable.

Thus, in Example V, *Weers et al.* does refer to powders which incorporate a poorly soluble active (Budesonide), but this Example **incorporates an excipient** (lactose monohydrate) thus teaching the opposite of the invention claimed by the applicants. Thus the specification teaches:

> The objective of this study was to examine the effect added calcium had on the physical stability of lipid-based pMDI suspensions to moisture. Budesonide powders were prepared by spray-drying a feed solution comprised of micronized drug particles suspended in the aqueous phase of a fluorocarbon-in-water emulsion. Accordingly, 0.8 g saturated egg phosphatidylcholine (EPC-3, Lipoid KG, Ludwigshafen, Germany) was dispersed in approximately 80 mL hot deionized water (T=80.degree. C.) using an Ultra-Turrax mixer at 8000 rpm for 2 to 5 minutes. 20 g of perflubron (.phi.=0.09) was then added drop wise during mixing. After the addition was complete, the emulsion was mixed for an additional period of not less than 4 minutes. The resulting coarse emulsion was homogenized under high pressure with an Avestin C-5 homogenizer (Ottawa, Canada) at 18,000 psi for 5 passes. The resulting submicron emulsion was then combined with **a second aqueous phase containing 1.33 g budesonide suspended in a solution comprising 0.4 g d-lactose monohydrate, and 0-0.134 g calcium chloride dissolved in approximately 30 g of deionized water.** The combined solution was then mixed using an Ultra-Turrax mixer at 8000 rpm for 2 minutes to ensure dispersion of the budesonide particles. Hollow porous budesonide particles were prepared by spray-drying the dispersion with a B-191 Mini Spray-Drier (Buchi, Flawil, Switzerland) under the following spray conditions: aspiration=80%, inlet temperature=85.degree. C., outlet temperature=57.degree. C., feed pump=2.3 mL/min, total air flow=22.4 SCFM. Free flowing white powders were collected at the cyclone separator. Scanning electron microscopic (SEM) analysis showed the powders to be spherical and highly porous. [emphasis added]

Weers et al., Paragraph 0089.

Additionally, with regard to new claims 107-108, Weers et al teaches nothing with regard to Ostwald ripening, or the necessity of avoiding Ostwald ripening in particulates comprising **an insoluble or sparingly soluble active**, and engineered and intended for aerosolization and pulmonary delivery to a patient.

As the independent claims are allowable over the prior art of record, then their dependent claims are allowable as a matter of law, because these dependent claims contain all features/elements/steps of their respective independent claim. *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988). Additionally and notwithstanding the foregoing reasons for the allowability of independent claims 38, 54 and 104, the dependent claims recite

further features/steps and/or combinations of features/steps (as is apparent by examination of the claims themselves) that are patentably distinct from the prior art of record. Hence, there are other reasons why these dependent claims are allowable.

In view of the above, applicants respectfully request that these grounds of rejection be withdrawn.

Conclusion

In view of the foregoing, applicants submit that pending claims 38-39, 41, 44, 47-56, 58, 60, 62-68, 103-105, and 107-108 satisfy the requirements of patentability and are therefore in condition for allowance. Reconsideration and withdrawal of all rejections is respectfully requested and a prompt mailing of a Notice of Allowance is solicited.

If a telephone conference would expedite the prosecution of the subject application, the Examiner is requested to call the undersigned at (650) 283-6790.

Respectfully submitted,
Nektar Therapeutics

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By: _____
Michael J. Mazza
Registration No. 30,775

CORRESPONDENCE ADDRESS:
Customer No. 21968

Nektar Therapeutics
201 Industrial Road
San Carlos, CA 94070
650-631-3100 (Telephone)
650-620-6395 (Facsimile)